Research Ethics Committee (Human)
Jawatan Kuasa Etika Penyelidikan (Manusia) - [JEPeM]

Background

The Human Research Ethics Committee of USM (JEPeM) started as JEPEM, established under the medical school [PPSP] administration in 1987. The initial responsibility was to review and vet research proposals for short and long term research grants. Its role was later expanded to include vetting on ethical issues as PPSP embarked on clinical trials in 1994. The committee was initially catering for research proposals from PPSP.

In 2002, the Committee was made the only human ethics committee for University Sains Malaysia. This Research and Ethical Committee is listed under the Office for Human Research Protections (OHRP), United States Department of Health & Human Services, since October 2004 as we began to do more clinical trials involving international pharmaceutical companies The Federal-wide Assurance (FWA) identification number is FWA00007718 and the Institutional Review Board (IRB) number is IRB00004494. The term of accreditation is until April 2011. The Committee adopts research ethics guidelines outlined by the Helsinki Declaration agreed by the World Medical Association and Council for International Organizations of Medical Sciences (CIOMS).

Clinical Science Research Platform [CSRP] was established in 2004. Its role is to facilitate and mobilize clinical researches. JEPEM was then transferred under the administration of CSRP in April 2007 and renamed JEPeM.

Terms of Reference of JEPeM

To vet and regulate clinical proposals on;

- Research involving human subjects [patients or normal people]
- Research involving human samples
- Research involving data derived from humans
- Research using products [biological or non-biological] which will be tested on humans

Research Ethics Committee - according to Helsinki Declaration – CIOMS

(a) Chairperson; The chairperson should be chosen for her or his ability to draw on the experience of all members, including lay members and those with specialist expertise, and to demonstrate respect for each member's view. The chairperson also has responsibility for managing the agenda and making sure that all relevant items are covered and adequately recorded.

(b) Lay members: at least two members who are lay people, one man and one woman, who have no affiliation with the institution or organisation, are not currently involved in medical, scientific, or legal work, and who are preferably from the community in which the institution or organisation is located. The qualifications for lay members are their independence from the institution and their non-involvement in medical, scientific or legal work. Those recruited from the community in which the institution is located are more likely to understand that community and how its members would view involvement in research. And those who have no experience in professions associated with research on human beings are more likely to bring a truly lay perspective.

(c) At least one member with knowledge of, and current experience in, the areas of research.

(d) At least one member with knowledge of, and current experience in, the professional care, counseling or treatment of people (e.g. medical practitioner, clinical psychologist, social worker, nurse, as appropriate). There may need to be more than one member in this category. This category of member is included because such a person has contact with potential or typical participants in research and has insights into the possible impact of research on such people.

(e) At least one member who is a minister of religion, or a person who performs a similar role in a community such as religious elder. This person holds some knowledge on multi-religions /cultures issues.

(f) At least one member who is a lawyer. This member should have professional qualifications but need not be currently in legal practice. The role of the lawyer on an ethics committee is to 'advise the committee on legal implications of research considered or decisions taken and whether formal legal advice is necessary.

General Guidelines of Ethical Research

The main principles of medical ethics, which JEPeM members must uphold, are:

i. Beneficence, or the duty to promote the good of the patient, subservient only to the larger good of the community;
ii. Autonomy, which is respect for the patient's rights to self-determination;
iii. Non-malfeasance, i.e. the duty not to inflict harm or injury, which should always be considered together with beneficence; and
iv. Justice, i.e. the patient should be given what are his or her due, within the limits of legal or societal concerns.

JEPeM members should also take note that the investigator(s) is/are appropriately qualified and experienced and commands facilities to ensure that all aspects of the work will be undertaken with due discretion and precaution to protect the safety of the subjects.

Adequate preliminary literature and experimental studies should have been undertaken to define, as far as practicable, the risks inherent in participation, and the investigators should be fully conversant with these.

The following notes are useful to JEPeM members;

Scientific Quality

Badly planned, poorly designed research that cannot be expected to produce useful or valid results, is unethical. Full scientific evaluation is beyond the capacity of most Ethics Committees. JEPeM members should not hesitate to make use of external advisers when necessary.

Medical Practice Vs Medical Research

The distinction derives from the intent. In medical practice the sole intention is to benefit the individual patient consulting the clinician, not primarily to gain knowledge of general benefit, although such knowledge may incidentally emerge from the clinical experience gained. In medical research the primary intention is to advance knowledge so that patients in general may benefit; the individual patient may or may not benefit directly.

Innovative Therapy Vs Conventional Therapy

When a clinician departs in a significant way from standard or accepted practice entirely for the benefit of a particular patient, and with consent, the innovation need not constitute research, although it may be described as an experiment in the sense that it is novel and invalidated. (In this context an 'experiment' is a procedure adopted on the chance of its succeeding. 'Research' is a systematic investigation to establish facts or principles and generalisable knowledge.) However, extension of such an experiment into wider use or general application should, prima facie, be regarded as research. Clinicians should be prepared to justify their innovative therapy both ethically and scientifically.

There are two major classes of research:

i. that which involves making observations without any direct interference with the subject (non-intrusive or non-invasive), such as research involving the use of personal medical records;

ii. that which involves interference with the subject (psychological intrusion, including intrusion on privacy, or physical invasion). Such interference raises ethical issues, which may be large or very small - both should be subject to ethical review.

Ethical principles governing research

1. The research must conform to generally accepted moral and scientific principles.

2. The investigator must be mindful at all times of his or her duty towards the individual subject of the research respecting the subject's personality, rights, wishes, consent and freedom.

3. The research should be conducted only by suitably qualified persons having available facilities for the proper conduct of the work and for dealing with any emergency which may arise.

4. The subject or his or her legal guardian should have given free consent, after comprehending the nature of the study, before research is undertaken. The investigator is responsible for providing the subject or his or her guardian with sufficient information in language that he or she can understand about the purpose, methods, demands, risks, inconvenience and discomforts of the study.

5. The informed consent of the subject is mandatory in all human research projects. Evidence of consent should be obtained in writing in the case of research and experiments classified as involving risk above the everyday norm and more generally where there is reason to believe or reason to suspect that subjects are in a dependent relationship.

6. Participation in research must be voluntary but recompense may be made for inconvenience and time spent by volunteers.

7. Volunteers for research and experiments should ordinarily be called for by open advertisement, within or outside the University.

8. The subject or the subject's guardian must be free at any time to withdraw consent for further participation and to withdraw any unprocessed data previously provided.

9. The investigator should discontinue or modify the research if it becomes apparent that continuation may be harmful.

10. Where research is initiated in an overseas country [such as pharmaceutical drug trials] the research must comply with the requirements of JEPeM Statement as well as the laws of Malaysia.

Points to consider by JEPeM members before a decision to award ethical approval

- Does the research respect the inherent dignity of all the participants?

- Where the research involves a collectivity or collectivities as participants, how are those components respected at the level of the collectivity?

- Does the research involve participants who are competent to decide for themselves?

- Does the research involve participants whose capacity for making informed choices is impaired or who otherwise have diminished autonomy?

- How is the research designed to respect participants capable of making informed choices and also those with diminished autonomy?

- Have the risks and benefits of the research proposal been identified and fully evaluated? Do the potential benefits justify any risks?

- Where a research project involves vulnerable people as potential research participants, or those unable to make independent and considered decisions, have sufficient measures been included in the research proposal to protect these people from harm?

- Are there provisions in the research proposal for continuing review and monitoring of data regarding efficacy and safety of the ongoing research process?

INFORMED CONSENT

Before research is undertaken, whether involving individuals or collectivities, the consent of the Participants must be obtained.

The ethical and legal requirements of consent have two aspects: the provision of information and the capacity to make a voluntary choice. So as to conform to ethical and legal requirements, obtaining consent should involve:

(a) Provision to participants, at their level of comprehension, of information about the purpose, methods, demands, risks, inconveniences, discomforts, and possible outcomes of the research (including the likelihood and form of publication of research results); and

(b) The exercise of a voluntary choice to participate. Where a participant lacks competence to consent, a person with lawful authority to decide for that participant must be provided with that information and exercise that choice.

Points to consider by JEPeM members on Informed Consent

- Do the recruitment and decision-making processes included in the research proposal ensure adequate protection of the freedom of participants to decide whether or not to participate in the project?
- Do the recruitment processes included in the research proposal provide for a disclosure of the types of information listed in this paragraph?
- Are all participants likely to be competent to decide whether or not to participate? If not, how is this addressed in the research proposal?

RESEARCH MERIT AND SAFETY

Every research proposal must demonstrate that the research is justifiable in terms of its potential contribution to knowledge and is based on a thorough study of current literature as well as prior observation, approved previous studies, and where relevant, laboratory and animal studies. All research involving humans needs to have both value and validity.

Points to consider by JEPeM members on research merit and safety

- Is there a clear hypothesis?
- Is the research likely to yield new knowledge, enhance understanding or clarify existing uncertainty?
- Has this, or similar, research been carried out before in the same, or similar contexts?
- Could a systematic review of the literature demonstrate the importance of the research question?
- Do the researchers have the necessary expertise to analyse and interpret the results of the research project?
- Has a statistician been involved in the preparation of the research proposal? If not, should a statistician be consulted?
- Has the research project been designed to account for, or avoid, biases in participant selection, data collection, data analysis and data interpretation?

RECORDING OF DECISIONS by JEPeM

JEPeM shall maintain a record of all research protocols received and reviewed, including:

- Name of responsible institution or organisation;
- Project Identification number(s);
- Principal Researcher(s);
- Title of project;
- Ethical approval or non-approval with date;
- Approval or non-approval of any changes to the protocol;
- The terms and conditions, if any, of approval of any protocol.

MONITORING BY JEPeM

JEPeM has the responsibility to ensure that the conduct of all research approved is monitored to a certain extent although policing job is not possible.

JEPeM expect reports from principal researchers on:

(a) Progress to date or outcome in the case of completed research;

(b) Maintenance and security of records;

(c) Compliance with the approved protocol; and

(d) Compliance with any conditions of approval.

JEPeM also requires that researchers to immediately report anything which might warrant review of ethical approval of the protocol, including:

(a) Serious or unexpected adverse effects on participants;

(b) Proposed changes in the protocol; and

(c) Unforeseen events that might affect continued ethical acceptability of the project.

Serious adverse effect is defined as any untoward medical occurrence that at any dose:

(e) Results in death

(f) Life threatening

(g) Requires in-patient hospitalisation or prolongation of existing hospitalisation;

(h) Results in persistent or significant disability/incapacity; or

(i) Congenital anomaly/birth defect.

SUSPENSION OR DISCONTINUATION OF RESEARCH

Where JEPeM is satisfied that circumstances have arisen such that a research project is not being or cannot be conducted in accordance with the approved protocol and that, as a result, the welfare and rights of participants are not or will not be protected, JEPeM may withdraw approval, inform the researcher(s) and the institution(s) or organisation(s) of such withdrawal, and recommend to the institution(s) or organisation(s) that the research project be discontinued, suspended, or that other necessary steps be taken.

A researcher must not continue the research if ethical approval has been withdrawn and must comply with any special conditions required by JEPeM.

MULTI-CENTRE RESEARCH

Multi-centre research may include:

(a) a research project conducted at more than one institution or organisation either by the same or different researchers, e.g. A clinical drug trial;

(b) a research project conducted jointly by researchers affiliated with different institutions or organisations; and

(c) a research project being conducted by a researcher who changes affiliation from one institution or organisation to another.

It is important to recognise that there can be a great range of variation in the scale of a multi-centre research proposal. Multi-centre research ranges from large, internationally supported clinical trials involving many researchers and supported by vast resources to a PhD student in a three-year course wishing to administer a questionnaire to students in several universities. This is as much multi-centre research as is the large clinical trial. However, the PhD student may have limited resources and time and JEPeM needs to be aware of these limitations.

In order to minimise unnecessary duplication in review of multicentre research, JEPeM would want to know if the same protocol has been reviewed by another JEPeM, including reviews conducted overseas.

JEPeM should ask for information, within the format of their application form, on the identity of other JEPeMs that have been, are being, or will be asked to consider the research protocol (or one very similar in content) that is being submitted. They are entitled to rely on the obligation of researchers to provide this information.

RESEARCH INVOLVING CHILDREN AND YOUNG PEOPLE

Research involving children and young people should only be conducted where:

(a) the research question posed is important to the health and wellbeing of children or young people;

(b) the participation of children or young people is indispensable because information available from research on other individuals cannot answer the question posed in relation to children or young people;

(c) the study method is appropriate for children or young people; and

(d) the circumstances in which the research is conducted provide for the physical, emotional and psychological safety of the child or young person.

Consent to a child's or young person's participation in research must be obtained from:

(a) Compliance with any conditions of approval.

(b) the child or young person whenever he or she has sufficient competence to make this decision; and either the parents/guardian in all but exceptional circumstances; or

(c) any organisation or person required by law.

RESEARCH INVOLVING PERSON WITH AN INTELLECTUAL OR MENTAL IMPAIRMENT

When considering approval of research involving persons with an intellectual or mental impairment, JEPEM should weigh the potential benefits against risks and undue burden.

Consent to participation in research by a person with an intellectual or mental impairment must be obtained from:

(a) the person with the intellectual or mental impairment whenever the person is of sufficient competence and, where the impairment is temporary or recurrent, at a time when the impairment does not prevent the person giving or refusing consent; or, failing that,

(b) the person's guardian, or an authority or other organization or person having that responsibility at law.

RESEARCH INVOLVING PERSONS HIGHLY EPENDENT ON MEDICAL CARE

For those carrying out such research, there is a need to acknowledge that the giving of free and informed consent can be compromised by the effect of the medical condition on the person's capacity to form and express an opinion or to communicate. Additionally, there may be a perception of coercion if a person is reluctant to refuse consent in fear that it may compromise his or her medical treatment.

EMERGENCY CARE RESEARCH

The distinguishing feature of emergency care research is that consent for entry into a project usually has to be obtained rapidly, when the vulnerability of patients and families is likely to be greatest. Moreover, the circumstances surrounding emergency care research are such that it may not always be possible to obtain consent for inclusion from either the patient or next of kin without delaying the initiation of treatment, and so risking a reduction of potential benefits.

INTENSIVE CARE RESEARCH

The distinguishing features of intensive care research are the difficulty in communicating with patients receiving ventilatory assistance and the impairment of cognition in heavily sedated individuals. Whenever possible, information about and consent to intensive care research should be given to and sought from potential participants before admission to that care.

NEONATAL INTENSIVE CARE RESEARCH

The very small size and vulnerability to harm of some infants is a unique feature of this research which renders all but minimal intrusion likely to be contrary to the child's best interests. The collection of even small blood samples additional to those required for diagnostic purposes or handling of a low birth weight infant to make observations will demand careful scrutiny.

TERMINAL CARE RESEARCH

Research in terminal care is distinguished by the short remaining life expectancy of participants and their potential vulnerability to unrealistic expectations of benefits. Researchers must take care that the prospect of benefit from research participation is neither exaggerated nor used to justify a higher risk than that involved in the patient's current treatment. Researchers must respect the needs and wishes of participants to spend time as they choose, particularly with family members.

COMMUNICATION

The distinguishing features of research involving persons with impaired capacity for communication include situations where the impairment is an acute state requiring dependence on medical care as well as non-acute states. In the former, the condition and medical care can mask their degree of cognition and require different means to express known wishes. In the latter, the condition may be such as to prevent the person expressing wishes.

RESEARCH INVOLVING HUMAN TISSUE

Biomedical research using human tissue samples has played a significant role in advancing medical scientific knowledge and contributing to our understanding of the causes and management of a wide range of diseases. Clearly, medical science and the community as a whole have benefited from these efforts. However, in recent years, a number of factors have led to attention being focused on ethical questions arising from procedures employed for collecting human tissue as research material. These include the rapid increase in medical research activity in recent years and the growing number of commercial applications for its outcomes.

FACTORS FOR CONSIDERATION ON RESEARCH INVOLVING HUMAN TISSUE

(a) the original reason for which the tissue is collected - that is, whether it is donated for the purpose of research or removed as part of a medical procedure performed for a therapeutic purpose.

(b) the timing of tissue collection in relation to the research - that is, whether the tissue to be used has been collected previously, as in the case of stored samples, or whether it is to be collected prospectively;

(c) the nature and amount of tissue, for example, whether it is regenerative or nonregenerative or whether it is a blood sample or organ biopsy;

(d) the research use to which the tissue will be put - that is, whether this will be epidemiological, non-identifying use, or identifying use, given that the results of such research may have consequences for the donor or the donor's family.

(e) potential commercial applications for research outcomes and whether the donor, or an authorised third party, understands and approves of the research and its objectives issues of religious and cultural sensitivity to the collection, storage and use of particular human tissue samples.

COMMERCIAL DEVELOPMENT OF TISSUE SAMPLES AND CONSENT

Potential tissue donors/research participants should be provided with all information about the possible uses and outcomes of the research during the consent process. If there is a possibility of commercialisation, and the person has been informed of this, they can make an informed choice about whether to be involved. Most donors choose to donate for altruistic or non-commercial reasons.

STORAGE OF TISSUE AND CONSENT

If a participant's tissue is to be stored after the completion of a research project, they should be informed of this beforehand. Participants should also be told if the purpose of storing their tissue is for use in future research. If the participant expresses a wish that their tissue not be employed in further research purposes, or for specific types of research, their decision should be respected. Where a tissue sample is not to be used for further research, researchers should honour the wishes of the participant (if any were expressed at the time of consent) with regard to the disposal of the sample. Some participants or collectivities will have sensitivities in this area.

WAIVER OF CONSENT ON RESEARCH USING HUMAN TISSUES

This applies particularly to stored material that has previously been used in research. JEPeM needs to consult relevant consent documents and decide whether the original consent given by the donor is in the spirit of the new research. The justification presented for seeking waiver of consent, including the extent to which it is impossible or difficult or intrusive to obtain specific consent. In some situations it will be impossible, or extremely difficult, for researchers to obtain the consent of the original donors for the use of stored tissue samples. Tissue from an archaeological site is an obvious example. This provision would also apply where the samples may have been stored for a long time and the donors are untraceable or have died, or it may be excessively difficult for other reasons to trace the donors. If a situation arises, JEPeM may approve the use of these samples, provided they are used in a de-identified [anonymous] form.

Where it is technically impossible to de-identify the stored tissue sample, the committee may approve its use in a potentially identifiable form. However, in this case, protection of the codes becomes important. The committee will need to decide whether the code that links the information and material to the identifiers should be held by the researchers or by a third party.

In some situations, JEPeM may believe that the procedures required to obtain consent are likely to cause unnecessary anxiety for those whose consent would be sought. This may be applicable in situations where tissue samples are accessed by authorised persons and identifiable data removed before the researcher gets access to the data. To require consent in this case would violate the privacy of research participants.

The proposed arrangements to protect privacy, including the extent to which it is possible to de-identify the sample If an JEPeM waives the requirement for consent it should particularly ensure that the researchers have adequate experience and resources to maintain privacy. If possible, the tissue should be used in de-identified form.

A lack of identifiers also makes it impossible for researchers to directly offer potential benefits of the study to donors or their families. This may be a particularly relevant issue in situations where researchers detect indicators of a medical condition where early intervention might be beneficial. If this is judged likely to occur, the JEPeM may require procedures to allow participants to be identified to facilitate appropriate follow-up. In this case, the researcher should also show due consideration in the research protocol of a plan to manage the disclosure of such information to participants, including access to medical advice or counseling.

DNA ANALYSIS

The issue of genetic research [DNA analysis] MUST not be done without consent. Thus if there is any intention of doing genetic analysis on identifiable material, consent for this must be obtained at the time the sample is taken (otherwise as soon as possible after the decision to do the analysis is taken).

CONCLUSION

This paper proposes Jawatan Kuasa Etika Penyelidikan to be placed under the administration of Clinical Research Dean. The current JEPEM under PPSP should now be separated and renamed JEPeM [**J**awatankuasa **E**tika **Pe**nyelidikan **M**anusia]

REFERENCES

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